CLAIMS

We claim:

1. An isolated polypeptide comprising a sequence of amino acid residues that is at least 90% identical to residues 41 (Gln) to 148 (Ile) as shown in SEQ ID NO: 2, wherein the residue at position 44 is Asp, the residue at position 47 is Asp and the residue at position 135 is Glu.

2. The isolated polypeptide of claim 1, wherein amino acid residues 71, 78, 122 and 125 are cysteine.

3. The isolated polypeptide of claim 1, wherein the sequence of amino acid residues is at least 95% identical to SEQ ID NO: 2, from residues 41 (Gln) to 148 (Ile).

4. The isolated polypeptide of claim 1, wherein the sequence of amino acid residues is 100% identical to SEQ ID NO: 2 from residues 41 (Gln) to 148 (Ile).

5. The isolated polypeptide of claim 1, wherein the polypeptide binds the zalpha11 receptor as shown in SEQ ID NO: 115.

6. An isolated polypeptide comprising a sequence of amino acid residues as shown in SEQ ID NO: 2 from residue 32 (Gln) to residue 162 (Ser) or as shown in SEQ ID NO: 56 (Mouse) from residue 23 (Gln) to residue 146 (Ser).

7. The isolated polypeptide of claim 6, wherein the sequence of amino acid residues as shown in SEQ ID NO: 2 is residue 1 (Met) to residue 162 (Ser) or as shown in SEQ ID NO: 56 (Mouse) is residue 1 (Met) to residue 146 (Ser).

8. An isolated polypeptide comprising at least 14 contiguous amino acid residues of SEQ ID NO: 2 or SEQ ID NO: 56.

9. The isolated polypeptide of claim 8, wherein the amino acid residues are selected from the group consisting of:

(a) amino acid residues 41-56 of SEQ ID NO: 2;

(b) amino acid residues 69-84 of SEQ ID NO: 2;

(c) amino acid residues 92-105 of SEQ ID NO: 2; and

(d) amino acid residues 135-148 of SEQ ID NO: 2.

10. A fusion protein comprising at least four polypeptides, wherein the order of polypeptides from N-terminus to C-terminus are:

a first polypeptide that comprises a sequence of amino acid residues from 41 to 56 of SEQ ID NO: 2;

a first spacer of 6-27 amino acid residues;

a second polypeptide that comprises a sequence of amino acid residues selected from the group consisting of:

(a) IL-2 helix B residues 53-75 of SEQ ID NO: 111;

(b) IL-4 helix B residues 65-83 of SEQ ID NO: 112;

(c) IL-15 helix B residues 84-101 of SEQ ID NO: 113;

(d) GMCSF helix B residues 72-81 of SEQ ID NO: 114; and

(e) amino acid residues 69-84 of SEQ ID NO: 2;

a second spacer of 5-11 amino acid residues;

a third polypeptide that comprises a sequence of amino acid residues selected from the group consisting of:

(a) IL-2 helix C residues 87-99 of SEQ ID NO: 111;

(b) IL-4 helix C residues 95-118 of SEQ ID NO: 112;

(c) IL-15 helix C residues 107-119 of SEQ ID NO: 113;

(d) GMCSF helix C residues 91-102 of SEQ ID NO: 114; and

(e) amino acid residues 92-105 of SEQ ID NO: 2;

a third spacer of 3-29 amino acid residues; and

a fourth polypeptide that comprises a sequence of amino acid residues selected from the group consisting of:

(a) IL-2 helix D residues 103-121 of SEQ ID NO: 111 ;

(b) IL-15 helix D residues 134-157 of SEQ ID NO: 112;

(c) IL-4 helix D residues 134-160 of SEQ ID NO: 113;

(d) GMCSF helix D residues 120-131 of SEQ ID NO: 114; and

(e) amino acid residues 135-148 of SEQ ID NO: 2.

11. A fusion protein comprising at least four polypeptides, wherein the order of polypeptides from N-terminus to C-terminus are:

a first polypeptide that comprises a sequence of amino acid residues selected from a group consisting of:

(a) IL-2 helix A residues 36-46 of SEQ ID NO: 111;

(b) IL-4 helix A residues 29-43 of SEQ ID NO: 112;

(c) IL-15 helix A residues 45-68 of SEQ ID NO: 113;

(d) GMCSF helix A residues 30-44 of SEQ ID NO: 114; and

(e) amino acids residues 41-56 of SEQ ID NO: 2;

a first spacer of 6-27 amino acid residues;

a second polypeptide that comprises a sequence of amino acid residues selected from the group consisting of:

(a) IL-2 helix B residues 53-75 of SEQ ID NO: 111;

(b); IL-4 helix B residues 65-83 of SEQ ID NO: 112;

(c) IL-15 helix B residues 84-101 of SEQ ID NO: 113;

(d) GMCSF helix B residues 72-81 of SEQ ID NO: 114; and

(e) amino acid residues 69-84 of SEQ ID NO: 2;

a second spacer of 5-11 amino acid residues;

a third polypeptide that comprises a sequence of amino acid residues selected from the group consisting of:

(a) IL-2 helix C residues 87-99 of SEQ ID NO: 111;

(b) IL-4 helix C residues 95-118 of SEQ ID NO: 112;

(c) IL-15 helix C residues 107-119 of SEQ ID NO: 113;

(d) GMCSF helix C residues 91-102 of SEQ ID NO: 114; and

(e) amino acid residues 92-105 of SEQ ID NO: 2;

a third spacer of 3-29 amino acid residues; and

a fourth polypeptide that comprises a sequence of amino acid residues from 135-148 of SEQ ID NO: 2.

12. A fusion protein according to claim 10, wherein the fourth polypeptide comprises amino acid residues 135-148 of SEQ ID NO: 2.

13. An isolated polynucleotide molecule comprising a sequence of nucleotides that encode the polypeptide of claim 1.

14. The isolated polynucleotide molecule of claim 13, wherein the nucleotides are as shown in SEQ ID NO: 1 from nucleotide 167 to nucleotide 490 or as shown in SEQ ID NO: 3 from nucleotide 121 to nucleotide 444.

15. An isolated polynucleotide molecule comprising a sequence of nucleotides that encode for the polypeptide of claim 8.

16. An isolated polynucleotide molecule comprising a sequence of nucleotides that encode the polypeptide as shown in SEQ ID NO: 2 from residue 32 to residue 162 or as shown in SEQ ID NO: 56 from residue 23 to residue 146.

17. The isolated polynucleotide molecule of claim 16, wherein the nucleotides are as shown in SEQ ID NO: 1 from nucleotide 140 to nucleotide 532 or as shown in SEQ ID NO: 3 from nucleotide 94 to nucleotide 486.

18. An isolated polynucleotide molecule comprising a sequence of nucleotides that encode the polypeptide as shown in SEQ ID NO: 2 from residue 1 to residue 162 or as shown in SEQ ID NO: 56 from residue 1 to residue 146.

19. The isolated polynucleotide molecule of claim 18, wherein the nucleotides are as shown in SEQ ID NO: 1 from nucleotide 47 to nucleotide 532 or as shown in SEQ ID NO: 3 from nucleotide 1 to nucleotide 486.

20. An expression vector comprising the following operably linked elements:

(a) a transcription promoter;

(b) a DNA segment encoding a polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) amino acid residues 41-56 of SEQ ID NO: 2;

(b) amino acid residues 69-84 of SEQ ID NO: 2;

(c) amino acid residues 92-105 of SEQ ID NO: 2; and

(d) amino acid residues 135-148 of SEQ ID NO: 2; and

(c) a transcription terminator.

21. An expression vector comprising the following operably linked elements:

(a) a transcription promoter;

(b) a DNA segment encoding a polypeptide comprising a sequence of amino acid residues that is at least 90% identical to residues 41 (Gln) to 148 (Ile) as shown in SEQ ID NO: 2, wherein the residue at position 44 is Asp, the residue at position 47 is Asp and the residue at position 135 is Glu; and

(c) a transcription terminator.

22. An expression vector comprising the following operably linked elements:

(a) a transcription promoter;

(b) a DNA segment encoding a polypeptide comprising amino acid residues 32 (Gln) to 162 (Ser) of SEQ ID NO: 2; and

(c) a transcription terminator.

23. A cultured cell comprising the expression vector according to any one of claims 20, 21 or 22.

24. A method of producing a protein comprising:

culturing a cell according to claim 23 under conditions wherein the DNA segment is expressed; and

recovering the protein encoded by the DNA segment.

25. A method of producing an antibody to a zalpha11 Ligand polypeptide comprising:

inoculating an animal with a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of 9 to 131 amino acids, wherein the polypeptide is identical to a contiguous sequence of amino acid residues in SEQ ID NO:2 from amino acid number 32 (Gln) to amino acid number 162 (Ser);

(b) a polypeptide according to claim 1;

(c) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 41 (Gln) to amino acid number 148 (Ile);

(d) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 41 (Gln) to amino acid number 56 (Val);

(e) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 69 (Thr) to amino acid number 84 (Leu);

(f) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 92 (Asn) to amino acid number 105 (Arg);

(g) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 135 (Glu) to amino acid number 148 (Ile);

(h) a polypeptide comprising the amino acid sequence of SEQ ID NO:72;

(i) a polypeptide comprising the amino acid sequence of SEQ ID NO:73;

(j) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 32 (Gln) to amino acid number 162 (Ser);

(k) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 162 (Ser);

(l) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 114 to amino acid number 119;

(m) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 101 to amino acid number 105;

(n) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 126 to amino acid number 131;

(o) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 113 to amino acid number 118;

(p) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 from amino acid number 158 to amino acid number 162; and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

26. An antibody produced by the method of claim 25, wherein the antibody binds to a zalpha11 Ligand polypeptide.

27. An antibody which specifically binds to a polypeptide of claim 1.

28. A method of stimulating an immune response in a mammal exposed to an antigen or pathogen comprising the steps of:

(1) determining directly or indirectly the level of antigen or pathogen present in said mammal;

(2) administering a composition comprising zalpha11 Ligand polypeptide in an acceptable pharmaceutical vehicle;

(3) determining directly or indirectly the level of antigen or pathogen in said mammal; and

(4) comparing the level of the antigen or pathogen in step 1 to the antigen or pathogen level in step 3, wherein a change in the level is indicative of stimulating an immune response.

29. The method of claim 28, further comprising:

(5) re-administering a composition comprising zalpha11 Ligand polypeptide in an acceptable pharmaceutical vehicle;

(6) determining directly or indirectly the level of antigen or pathogen in said mammal; and;

(7) comparing the number of comparing the antigen or pathogen level in step 1 to the antigen level in step 6, wherein a change in the level is indicative of stimulating an immune response.

30. The method according to one of claims 28 or 29, wherein the antigen is a B cell tumor; a virus; a parasite or a bacterium.

31. A method for expansion of hematopoietic cells and hematopoietic cell progenitors comprising culturing bone marrow or peripheral blood cells with a composition comprising an amount of zalpha11 Ligand sufficient to produce an increase in the number of lymphoid cells in the bone marrow or peripheral blood cells as compared to bone marrow or peripheral blood cells cultured in the absence of zalpha11 Ligand.

32 The method of claim 31, wherein the hematopoietic cells and hemopoietic progenitor cells are lymphoid cells.

33. The method of claim 32, wherein the lymphoid cells are NK cells or cytotoxic T cells.

34. The method of claim 31, wherein the composition also comprises at least one other cytokine selected from the group consisting of IL-2, IL-15, IL-4, GM-CSF, Flt3 ligand and stem cell factor.

35. A method of reducing proliferation of neoplastic B or T cells comprising administering to a mammal with a B or T cell neoplasm an amount of a composition of zalpha11 Ligand sufficient to reduce proliferation of the neoplastic B or T cells.

36. The method of claim 35 wherein the composition also comprises at least one other cytokine selected from the group consisting of IL-2, IL-15, IL-4, GM-CSF, Flt3 ligand or stem cell factor.

37. A method of reducing proliferation of neoplastic B or T cells comprising administering to a mammal with a B or T cell neoplasm an amount of a composition of zalpha11 Ligand antagonist sufficient to reducing proliferation of the neoplastic B or T cells.

38. The method of claim 37, wherein the composition also comprises at least one other cytokine selected from the group consisting of IL-2, IL-15, IL-4, GM-CSF, Flt3 ligand or stem cell factor.

39. The method of claim 37, wherein the zalpha11 Ligand antagonist is ligand/toxin fusion protein.

40. A method of stimulating an immune response in a mammal exposed to an antigen or pathogen comprising:

(1) determining a level of an antigen- or pathogen-specific antibody;

(2) administering a composition comprising zalpha11 Ligand polypeptide in an acceptable pharmaceutical vehicle;

(3) determining a post administration level of antigen- or pathogen-specific antibody;

(4) comparing the level of antibody in step (1) to the level of antibody in step (3), wherein an increase in antibody level is indicative of stimulating an immune response.

DS Rule 26 41 ~~42.~~ A method of detecting the presence of zalpha11 Ligand RNA in a biological sample, comprising the steps of :

(a) contacting a zalpha11 Ligand nucleic acid probe under hybridizing conditions with either (i) test RNA molecules isolated from the biological sample, or (ii) nucleic acid molecules synthesized from the isolated RNA molecules, wherein the

probe has a nucleotide sequence comprising either a portion of the nucleotide sequence of the nucleic acid molecule of claim 18, or its complement, and

(b) detecting the formation of hybrids of the nucleic acid probe and either the test RNA molecules or the synthesized nucleic acid molecules,

wherein the presence of the hybrids indicates the presence of zalpha11 Ligand RNA in the biological sample.

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42 ~~43.~~ A method of detecting the presence of zalpha11 Ligand in a biological sample, comprising the steps of:

(a) contacting the biological sample with an antibody, or an antibody fragment, of claims 26 or 27, wherein the contacting is performed under conditions that allow the binding of the antibody or antibody fragment to the biological sample, and

(b) detecting any of the bound antibody or bound antibody fragment.

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